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1: Proc Natl Acad Sci U S A. 1992 Dec 15;89(24):11949-53. Related Articles, Links

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Detection of glutamine synthetase in the cerebrospinal fluid of Alzheimer diseased patients: a potential diagnostic biochemical marker.

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In this report, 8- and 2-azidoadenosine 5'-[gamma-32P]triphosphate were used to examine cerebrospinal fluid (CSF) samples for the presence of an ATP binding protein unique to individuals with Alzheimer disease (AD). A 42-kDa ATP binding protein was found in the CSF of AD patients that is not observed in CSF from normal patients or other neurological controls. The photolabeling is saturated with 30 microM 2-azidoadenosine 5'-[gamma-32P]triphosphate. Photoinsertion can be totally prevented by the addition of 25 microM ATP. Photoinsertion of 2-azidoadenosine 5'-triphosphate into the protein is only weakly protected by other nucleotides such as ADP and GTP, indicating that this is a specific ATP binding protein. A total of 83 CSF samples were examined in a blind manner. The 42-kDa protein was detected in 38 of 39 AD CSF samples and in only 1 of 44 control samples. This protein was identified as glutamine synthetase [GS; glutamate-ammonia ligase; L-glutamate:ammonia ligase (ADP-forming), EC 6.3.1.2] based on similar nucleotide binding properties, comigration on two-dimensional gels, reaction with a polyclonal anti-GS antibody, and the presence of significant GS enzyme activity in AD CSF. In brain, GS plays a key role in elimination of free ammonia and also converts the neurotransmitter and excitotoxic amino acid glutamate to glutamine, which is not neurotoxic. The involvement of GS, if any, in the onset of AD is unknown. However, the presence of GS in the CSF of terminal AD patients suggests that this enzyme may be a useful diagnostic marker and that further study is warranted to determine any possible role for glutamate metabolism in the pathology of AD.

PMID: 1361232 [PubMed - indexed for MEDLINE]

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1: Brain Res. 1995 Mar 27;675(1-2):75-82.

Complement C1 inhibitor is produced by brain tissue and is cleaved in Alzheimer disease.

Walker DG, Yasuhara O, Patston PA, McGeer EG, McGeer PL.

Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, Canada.

C1 inhibitor was identified in human brain tissue by Western blotting and by immunohistochemistry using multiple antibodies to the native protein. The presence of C1 inhibitor mRNA was identified by reverse transcriptase-polymerase chain reaction analysis of brain mRNA extracts. The mRNA was also detected in cultured postmortem human microglia and in the IMR-32 human neuroblastoma cell line. Immunohistochemically, the native protein was detected in residual serum of capillaries and pyramidal neurons of both control and Alzheimer disease cases, as well as in occasional senile plaques of Alzheimer tissue. The reacted protein was detected on dystrophic neurites and neuropil threads in Alzheimer tissue by 4C3 monoclonal antibody, which recognizes a neoepitope following suicide inhibition. These data indicate that C1 inhibitor, a regulatory molecule controlling multiple inflammatory proteolytic cascades, is produced in normal brain. In Alzheimer disease, C1 inhibitor undergoes a prominent reaction in abnormal neuronal processes, such as dystrophic neurites and neuropil threads.

PMID: 7796155 [PubMed - indexed for MEDLINE]

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Examiner copy
reference # 6

1: Am J Pathol. 1999 Mar;154(3):927-36.

Up-regulated production and activation of the complement system in Alzheimer's disease brain.

Yasojima K, Schwab C, McGeer EG, McGeer PL.

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We used reverse transcriptase-polymerase chain reaction and Western blotting techniques to measure the levels of complement mRNAs and their protein products in Alzheimer's disease (AD) brain compared with non-AD brain. mRNAs for C1q, C1r, C1s, C2, C3, C4, C5, C6, C7, C8, and C9 were detected in the 11 regions of brain that were investigated. The mRNA levels were markedly up-regulated in affected areas of AD brain. In the entorhinal cortex, hippocampus, and midtemporal gyrus, which had dense accumulations of plaques and tangles, C1q mRNA was increased 11- to 80-fold over control levels, and C9 mRNA 10- to 27-fold. These levels were substantially higher than in the livers of the same cases. Western blot analysis of AD hippocampus established the presence of all of the native complement proteins as well as their activation products C4d, C3d, and the membrane attack complex. These data indicate that high levels of complement are being produced in affected areas of AD brain, that full activation of the classical complement pathway is continuously taking place, and that this activation may be contributing significantly to AD pathology.

PMID: 10079271 [PubMed - indexed for MEDLINE]

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